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Blood Rheology and Renal Transplantation: An Intriguing Relationship for Assessing Cardiovascular Risk

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ABSTRACT

Renal transplant recipients (RTRs) are at increased risk of cardiovascular complications. An altered hemorheological profile may determine both cardiovascular complications and progression of renal failure in RTRs. We performed this study to evaluate the rheologic status in 239 RTRs at least 12 months after transplantation with stable and normal renal function compared with 90 control subjects. In RTRs, a significantly higher hematocrit-adjusted, but not native, whole blood viscosity was found ($P < .0001$). Moreover, plasma viscosity and red blood cell deformability were significantly higher in patients than in control subjects ($P < .0001$), whereas no difference in erythrocyte aggregation between patients and control subjects was observed ($P = .5$). Fibrinogen, but not hematocrit, significantly increased in RTRs ($P = .001$). This preliminary study provides evidence of an altered hemorheologic profile in RTRs.

Cardiovascular disease is the main cause of mortality and morbidity in transplant recipients. Traditional risk factors, such as smoking habit, hypertension, dyslipidemia, and diabetes, do not completely account for the high incidence of cardiovascular risk in these patients. Novel markers of cardiovascular risk, such as an altered hemorheologic profile may influence cardiovascular mortality in these patients. Clinical studies[1] provided evidence that abnormalities in blood flow properties may contribute to cardiovascular events, and an altered hemorheologic profile, which worses microcirculatory blood flow and influences vascular disease, might determine both cardiovascular complications and progression of renal failure in renal transplant recipients (RTRs). Few data are available concerning the impact of blood rheology in affecting cardiovascular risk in RTRs.[2,3] We performed the present study to investigate the rheologic status in RTR patients at least 12 months after transplantation with stable and normal renal function.

METHODS

We investigated 239 RTR patients at least 12 months after transplantation with stable and normal renal function [156 men, median age 53 (range 17–75) y; 83 women, median age 50 (range 17–74) y] compared with 90 control subjects [38 men, median age 38 (range 22–63) y; 52 women, median age 41 (range 26–61) y] with no history of renal or cardiovascular disease. Patients and control subjects gave their informed consents and the study was approved by the local Ethics Committee. Hemorheologic profile was performed by assessing both whole-blood viscosity (at shear rates of 0.512 and 94.5/s), plasma viscosity, erythrocyte deformability and aggregability, and coagulation parameters (hemoglobin, hematocrit, and fibrinogen concentrations) as previously described.[4]

Statistical Analysis

Data are reported as mean ± SD and median (range) for nonparametric parameters, and the comparison between patients and controls was performed with the Mann-Whitney U test. All probability values were two tailed, with values of $<.05$ considered to be statistically significant.

RESULTS

In RTRs, a significantly higher hematocrit-adjusted, but not native, whole blood viscosity was found ($P < .0001$). Moreover, plasma viscosity and red blood cell deformability were significantly different between patients and control

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subjects ($P < .0001$), whereas no difference in erythrocyte aggregation between patients and controls subjects was observed ($P = .5$). Fibrinogen, but not hematocrit, significantly increased in RTRs ($P = .001$). Significantly lower hemoglobin values were observed in RTRs than in control subjects ($P < .0001$).

DISCUSSION

This study provides evidence of an altered hemorheologic profile in RTRs compared with healthy subjects. In particular, we observed a significant difference in hematocrit-adjusted whole blood viscosity and in both plasma viscosity and erythrocyte deformability, which is known to influence blood rheology. Of interest, the finding of a higher hematocrit-adjusted whole blood viscosity is in line with clinical data that in patients with chronic kidney disease, an early complete correction of anemia did not reduce the risk of cardiovascular events.[5] RTRs are known to be at greatly increased risk of cardiovascular morbidity and mortality compared with the general population,[6] and have an increased incidence of atherosclerotic plaques and other vascular alterations compared with control subjects.[7,8] Traditional risk factors, such as hypertension, smoking habit, diabetes, and dyslipidemia, are well known to increase the risk of cardiovascular disease in RTRs and thus possibly predict the incidence of cardiovascular events. Accordingly, an altered rheologic profile, which is known to influence cardiovascular risk,[1] may contribute to implement the risk profile panel in RTRs. In conclusion, our findings might suggest a contribution in assessing cardiovascular risk in RTRs to prevent cardiovascular complications. Nevertheless, further studies are required to confirm this preliminary data. A tailored pharmacologic intervention, aimed to correct the rheologic milieu, might permit reducing cardiovascular risk in these patients.

REFERENCES

1. Lowe GD: Can haematological tests predict cardiovascular risk? The 2005 Kettle Lecture. Br J Haematol 133:232, 2006

2. Linde T, Sandhagen B, Backman U, et al: Altered flow properties of blood and increased plasma fibrinogen in cyclosporin-treated renal allograft recipients. Nephrol Dial Transplant 14:1525, 1999

3. Koppensteiner R, Derfler K, Ehringer H: Blood rheology after renal transplantation. Nephron 74:328, 1996

4. Mannini L, Paniccia R, Cecchi E, et al: Reduced erythrocyte deformability and hypercoagulability in idiopathic sudden sensorineural hearing loss. Clin Hemorheol Microcirc 33:47, 2005

5. Drüeke TB, Locatelli F, Clyne N, et al, CREATE Investigators: Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med 355:2071, 2006

6. Marcén R: Cardiovascular risk factors in renal transplantation—current controversies. Nephrol Dial Transplant 21(suppl 3):iii3, 2006

7. Suwelack B, Witta J, Hausberg M, et al: Studies on structural changes of the carotid arteries and the heart in asymptomatic renal transplant recipients. Nephrol Dial Transplant 14:160, 1999

8. Barbagallo CM, Pinto A, Gallo S, et al: Carotid atherosclerosis in renal transplant recipients: relationships with cardiovascular risk factors and plasma lipoproteins. Transplantation 67:366, 1999